

REMARKS

With the entry of the present amendments, Claims 1, 3-21, 33, 55-62, 73-83, and 85-90 are pending in the application. Claims 21 and 55 are currently amended. Claims 63-72 and 84 have been canceled. Claims 2, 22-32, and 34-54 were canceled in a previous reply. New Claims 85-90 have been added. Support for the claim amendments and the new claims may be found throughout the application as filed, including but not limited to:

Claims 55 and 85: Paragraphs 0145-0148, 0152 and 0153;

Claim 86: Paragraphs 0032, 0143 (Example 10) and 0155-0157 (Example 12), and 0162-0172 (Examples 13-15);

Claim 87: Paragraph 0032 and 1055-0157; and

Claim 88-90: Paragraph 0154.

In view of the following remarks, reconsideration and withdrawal of the rejections to the application in the Office Action is respectfully requested.

I. Allowed Claims

Applicants thank the Examiner for acknowledging that Claims 1, 3-21 and 33 have been allowed.

II. Rejection of claims under 35 U.S.C. § 112, first paragraph, for failure to comply with the written description requirement.

Claims 55-62, 69, and 73-84 were rejected under 35 U.S.C. § 112, first paragraph, for failure to comply with the written description requirement. In support of this rejection, the Examiner stated, "Overall, the claims encompass a genus of proteins which are highly variant in both structure and function. The disclosure of SEQ ID NO: 1-23 and 26-31 does not adequately describe the claimed genus because the genus encompasses polypeptides which differ significantly in structure and function from SEQ ID NO: 1-23 and 26-31. One of skill in the art

would conclude that applicant was not in possession of the claimed genus.” Applicants respectfully traverse.

Applicants respectfully submit that the genus of polypeptides recited in amended claim 55 is strictly circumscribed with respect to both structure and function and that Applicants were in possession of this entire genus at the time the invention was made.

The Examiner’s conclusion that the rejected claims do not comply with the written description requirements is based on alleged shortcomings in both the structural and functional limitations in the rejected claims. Applicants will address the alleged shortcomings with regard to the structure and function of the claimed polypeptides separately below.

Regarding the structural limitations to the claimed polypeptides the Examiner states:

It is noted that SEQ ID NO: 1-23 and 26-31 range in length from 6-10 amino acids. A single alteration of amino acid would be equivalent to a 10% to 12.5% difference. Further, the claim does not restrict the amino acid substitution to a specific residue, thus, all positions are subject to the conservative amino acid alteration.

Applicants respectfully disagree.

The claims do not encompass a genus of polypeptides which are highly variant in structure relative to the literal polypeptide sequences recited in the claims. The permitted variance between the claimed genus of polypeptides and a given literal polypeptide is strictly circumscribed because the genus includes only those polypeptides that differ from the literal polypeptide sequence by a single conservative amino acid substitution. The application clearly defines a conservative amino acid substitution as a substitution where one amino acid residue is replaced by another, biologically similar residue. (See, paragraph 0051.) In fact, the concept of conservative amino acid substitutions is well known. For example, the Biology-Online Dictionary defines “Conservative Substitution” as follows: “In a gene product, a substitution of one amino acid with another with generally similar properties (size, hydrophobicity, etc), such

that the overall functioning is likely not to be seriously affected." Thus, the vary nature of a *conservative* amino acid substitution limits the possible structural variation.

In the Office Action, the Examiner points to the difference in *structural identity* of the polypeptides belonging to the genus for a given literal polypeptide sequence. Specifically, the Examiner points out that a substitution of a single amino acid in a polypeptide composed of 8-10 amino acids would amount to a 10-12.5% difference in a structural identity of the polypeptide. Applicants respectfully submit that the actual degree of similarity between the members of the genus and the literal polypeptides with which they are associated is much greater than the difference in their structural identity would suggest. As one of skill in the art would recognize "structural identity" only takes into account the absolute number of amino acid residues that are substituted. Structural identity does not account for the nature of the amino acids being substituted. "Structural similarity" is a measure of the degree of similarity between two polypeptides that differ only by conservative substitutions. Unlike measurements of structural identity, measurements of structural similarity take the conservative nature of the amino acid substitutions into account. Generally, this involves scoring a conservative substitution as a partial substitution rather than a full mismatch, thereby adjusting the measurement of percent sequence identity upward. Because the amino acid substitutions of the claimed polypeptides are strictly limited to conservative substitutions, "structural similarity" is the appropriate measure in this case. Moreover, because each polypeptide in the genus for a given literal polypeptide sequence may differ from that literal polypeptide sequence by only a *single* conservative amino acid substitution, it is clear that the members of the genus have a very high structural similarity and, therefore, very little structural variation.

Applicants were in possession of the polypeptides of the structurally-circumscribed genus recited in the rejected claims at the time the invention was made. Applicants have not only identified the literal sequences for many member of the genus, but have also clearly explained the mean by which they were able to identify the conservative amino acid substitutions that provide the remaining members of the genus. Specifically, paragraph [0052] of the application provides

a specific example of a software program (LASERGENE) that was available at the time the invention was made that would enable Applicants to identify conservative amino acid substitutions for the literal polypeptides, and thereby identify the members of the genus.

Regarding claims 56-62, Applicants further note that the degree of allowed structural variation in the polypeptides of the claimed genus is even more strictly limited, either by the recitation of specific properties which the substituted amino acid residues must possess (e.g., hydrophobicity or polarity) or by the specification of particular amino acid residues which may be involved in a conservative substitution.

With regard to the functional limitations on the claimed polypeptides, the Examiner stated that the rejected claims were not limited by the recitation of a functional attribute of the variant polypeptide. The Examiner further asserted that the limitation of binding to malignant and non-malignant myeloid cells does not narrow the genus appropriately because myeloid cells encompass a large genus of cell types, which carry different cell surface proteins. In order to expedite the prosecution of this application, Applicants have amended Claim 55 to include the limitation that the polypeptides bind to very specific myeloid cells, namely acute myeloid leukemia cells. In view of this amendment, Applicants respectfully submit that the Examiner's allegations with regard to the lack of functional limitation in the claim has been overcome and respectfully request that this rejection be withdrawn.

Applicants acknowledge that the Examiner also identified allegedly conflicting data regarding the binding characteristics of some of the polypeptides in the specification. Without acknowledging the validity of the alleged inconsistencies, Applicants note that the functional limitation included in amended Claim 55 is not subject to the alleged inconsistencies identified by the Examiner. Therefore, amended Claim 55 and the claims that depend therefrom, comply with the enablement requirement under 35 U.S.C. § 112, first paragraph.

Thus, based on the limited nature of the structural and functional variations in the polypeptides included in the claimed genus and the availability and identification of software for

identifying conservative amino acid substitutions, it is clear that Applicants were in possession of the entire claimed genus at the time the invention was made. For this reason, Applicants respectfully request that this rejection be withdrawn.

III. Rejection of claims under 35 U.S.C. § 112, first paragraph, for failure to comply with the enablement requirement.

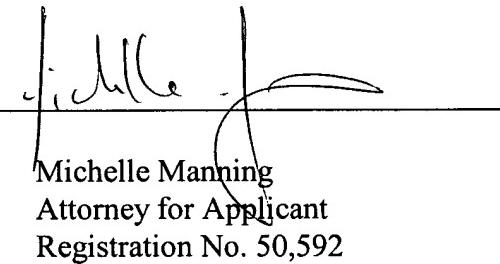
Claims 63-68 and 73-72 were rejected under 35 U.S.C. § 112, first paragraph, for failure to comply with the enablement requirement. In order to expedite the prosecution of this application, Claims 63-72 have been canceled, thereby rendering this rejection moot. For this reason, Applicants respectfully request that this rejection be withdrawn.

In view of the foregoing remarks, applicants respectfully submit that all of the claims remaining in the application are in condition for allowance and favorable action thereon is respectfully solicited.

Respectfully submitted,

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Dictionary



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conservative substitution

In a gene product, a substitution of one amino acid with another with generally similar properties (size, hydrophobicity, etc), such that the overall functioning is likely not to be seriously affected.

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